IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

APOTEX, INC., *Plaintiff* v. CEPHALON, INC., et al. *Defendants*	CIVIL ACTION No. 2:06-cv-2768-MSG

APOTEX INC.'S POST-TRIAL BRIEF
ON INVALIDITY AND INEQUITABLE CONDUCT

Introduction

Apotex's invalidity case is based on three fundamental principles of patent law. First, the '516 patent claims cover small modafinil compositions where 95% of the particles are smaller than 220 microns – that is it. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) ("[i]t is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude."). Second, those claims are invalid if Lafon Lot 5/2435 or Lot 003 (or any other small particle modafinil) is prior art because a specific example that falls within a claimed range anticipates that range. *Titanium Metals Corp. of Am. v. Banner*, 778 F.2d 775, 782 (Fed. Cir. 1985) ("It is also an elementary principle of patent law that when, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is 'anticipated' if one of them is in the prior art."); 4/6 T. Tr. at 146:17-22 (Cephalon's patent expert Mr. Stoner so admitting). Third, unexpected results, such as consistent dissolution (to the extent they exist), are irrelevant to anticipation. *In re Wiggins*, 488 F.2d 538, 543 (C.C.P.A. 1973); PTX-239 (MPEP at § 2131.04); 4/6 T. Tr. at 148:1-149:2 (Stoner so admitting, including that "the information in the Shek declaration, even if it's totally unexpected, could not overcome a 102 rejection").[1]

I. The "Invention" of the '516 Patent Is Defined By the Claims.

In determining validity (and materiality for inequitable conduct), the claims define the "invention" of the '516 patent that should be considered. *Phillips,* 415 F.3d at 1312. Claim 1 is simple as it covers any pharmaceutical composition (such as a tablet) with small modafinil:

[1] Below, Apotex addresses four bases for invalidity - anticipation under § 102(b) (on-sale bar); anticipation under § 102(f) (derivation); obviousness under § 103(a); and lack of written description under § 112 - as well as inequitable conduct. Given the strength of its other defenses and to save judicial resources, Apotex is no longer pursuing its public use or enablement claims. Apotex also addresses the standing issue again, as Cephalon raised it in its FRCP 52(c) motion. See Dkt. No. 449-1 at 9-10.

> 1. A pharmaceutical composition comprising a substantially homogeneous mixture of modafinil particles, wherein at least about 95% of the cumulative total of modafinil particles in said composition have a diameter of less than about 200 microns (μm).

JTX-1, Col. 10: 49-53. There are no limitations in any of the claims regarding bioavailability, dissolution, improved efficacy or safety, batch-to-batch consistency, or FDA specifications. *See* 3/29 T. Tr. at 100:10-101:4, 118:5-121:6 (Beach); 4/6 T. Tr. at 74:17-19 (Cooper); s*ee* JTX-4B at CPH_PLD_400-401 ("solubility and dissolution rates are not being claimed in this case. Nor are Applicants claiming a modafinil with a 'different' solubility profile or improved dissolution rate. What Applicants have discovered and what Applicants have claimed is modafinil of a defined particle size.") (emphasis added). The "invention" is just small particle modafinil.

II. Anticipation Law Generally.

Because the '516 patent claims all compositions with a 95% value less than 220 microns (covering each such example), it is anticipated if there is a *single* embodiment present in the prior art (such as seen in Lafon's modafinil Lots 003 and 5/2435). *See Titanium Metals*, 778 F.2d at 782; *Atlas Powder Co. v. IRECO, Inc.*, 190 F.3d 1342, 1346 (Fed. Cir. 1999) ("when a patent claims a chemical composition in terms of ranges of elements, any single prior art reference that falls within each of the ranges anticipates the claim"). This is true even if Cephalon "discovered" additional features of Lafon's modafinil because "the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder*, 190 F.3d at 1347; *Titanium Metals*, 778 F.2d at 782 (holding a patent claim to a titanium alloy with corrosion-resistant properties anticipated by a prior art alloy falling within the scope of the claims, even though the prior art did not disclose the corrosion resistant properties because "it is immaterial, on the issue of novelty, what inherent properties the alloys

have or whether these applicants discovered certain inherent properties."). Because small particle modafinil (e.g. Lot 003 and Lot 5/2435) was independently developed by Lafon[2] and sold to Cephalon pursuant to the Supply Agreement, it does not matter for anticipation if Cephalon "discovered" additional properties of that modafinil (e.g., the purported consistent dissolution rate), especially as they are not even claimed.[3]

III. The Claims of the '516 Patent are Invalid Under 35 U.S.C. § 102(b)("On-Sale Bar")

A. Legal Framework

A patent claim is invalid if "the invention was . . . on sale in this country, more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b); *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 424 F.3d 1276, 1281 (Fed. Cir. 2005).[4] Determining the on-sale bar is a conclusion of law based on underlying findings of fact. *Scaltech*, 269 F.3d at 1327. Under current Federal Circuit law, Apotex bears the burden of proving invalidity under on-sale bar (and for its other invalidity and unenforceability claims) by clear and convincing evidence.[5] A claimed invention is considered to be on sale under § 102(b) if two conditions are met prior to the critical date: it was (i) sold or the subject of a commercial offer for sale and (ii) ready for patenting. *See Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 67-68 (1998).[6]

---

[2] "Lafon" as used in the brief includes Lafon controlled facilities, such as Orsymonde and Macors, that made API and tablets . *See* Dkt. No. 438, Stipulations at ¶ 18.

[3] If the patent system awarded patents covering the product to persons who made additional discoveries about existing products, then company A could obtain a company B's product, make a new discovery on that product, get a patent covering that exact product, and exclude A from the market. *See* 4/1 T. Tr. at 168:2-21 (Gerstman referencing the "mischief" such a system would cause).

[4] "The date exactly one year prior to the date of application for the patent is known as the critical date" because it results in the barring activity under § 102(b). *See Scaltech, Inc. v. Retec/Tetra, L.L.C.*, 269 F.3d 1321, 1327 (Fed. Cir. 2001).

[5] Apotex believes that the Court should apply a preponderance of the evidence standard to its invalidity defenses, and adopts the arguments made by Microsoft in its petition to the Supreme Court. *See Microsoft Corp v. i4i Ltd. Partnership*, Dkt. No. 10-290, Microsoft's Petition for a Writ of Cert., 2010 WL 3413088 (August 27, 2010). Apotex also asserts that the same standard should be applied to its inequitable conduct defense for similar reasons.

[6] The on-sale bar requires the barring activity to be "in this country." 35 U.S.C. §102(b). Here, the on sale activity

B. First *Pfaff* Prong: The Supply Agreement and Lafon's Shipment of Tablets and API Were A Commercial Sale of Modafinil that Met the Limitations of the Asserted Claims

Section § 102(b) does not require that an embodiment of the invention actually be sold, only that it be "on sale." *Buildex Inc. v. Kason Indus., Inc.*, 849 F.2d 1461, 1464 (Fed. Cir. 1988). Because an offer to sell is all that is necessary, a contract to sell fully satisfies the "on sale" requirement. *Id.* The on-sale bar is not avoided just because the sale is contingent on another event. *See LaBounty Mfg. Inc. v. ITC*, 958 F.2d 1066, 1073-74 (Fed. Cir. 1992) (on-sale bar where the sale was contingent upon the customer's satisfaction with the product and provided a money-back guarantee); PTX-239 at 52 (MPEP § 2133.03(b)). Nor is there a requirement that the patented product actually be delivered prior to the critical date or that money change hands. *Weatherchem Corp. v. J.L. Clark, Inc.*, 163 F.3d 1326, 1333 (Fed. Cir. 1998). However, where it can be shown that an embodiment of the invention was delivered before the critical date, such delivery can be conclusive evidence that an offer for sale occurred. *Buildex*, 849 F.2d at 1464.

1. <u>The Lafon-Cephalon Supply Agreement was a commercial offer for sale of modafinil.</u>

The January 20, 1993 Supply Agreement (PTX-48) is a commercial offer for sale under the controlling Federal Circuit decision in *Enzo*, where the Federal Circuit affirmed a *summary judgment* that a similar agreement was a commercial offer for sale. 424 F.3d 1276. In *Enzo*, the contract included paragraph 2.14, which was a future supply requirement provision. *Id.* at 1279. In determining whether the agreement constituted a commercial offer for sale, the Federal Circuit paid "particular attention" to this provision and ultimately held:

---

was in this country because Cephalon is a U.S. based company, the Agreements refer to FDA approval in the U.S. and the Territory for the sale includes the U.S. *See* PTX-48 at CPH_PLD_23463; PTX-49 at CPH_PLD_23434; *see In re Caveney*, 761 F.2d 671, 676-77 (Fed. Cir. 1985) (an offer for sale originating in a foreign country, directed to a customer in the U.S., can establish an on-sale bar). Further, shipments of modafinil pursuant to the Supply Agreement, including Lot 003 API and M006 tablets, were received by Cephalon in the U.S. *See* PTX-66A. Cephalon has not challenged the "in this country" element.

> We agree with Gen-Probe that paragraph 2.14 of the Enzo-Ortho agreement created the necessary contractual obligations on the parties to constitute a commercial offer for sale. While it is true that the agreement states throughout its text that the parties are interested in cooperating in certain experimental work, the language of paragraph 2.14, unlike paragraph 2.12 and other provisions that explicitly refer to research and development efforts, does not purport to be for such preliminary production of the probe. Instead, paragraph 2.14 is distinctly different from those earlier sections because it relates specifically to supply of Ortho's worldwide requirements for what are clearly commercial purposes. Supply of worldwide requirements at reasonable times and prices ***surely*** means commercial supply, and the provision constitutes an offer to sell that has been accepted.

Id. at 1281-82 (citation and parenthetical omitted, emphases added).

In this case, the Supply Agreement is strikingly similar to the agreement found to be a commercial offer in *Enzo* because it is also a future supply requirements contract:

***Enzo* Agreement, Par. 2.14**	**PTX-48 Lafon Supply Agreement, Par. 3(b).**
2.14 ENZO shall supply to ORTHO and ORTHO shall purchase from ENZO for use in Licensed Products no less than ninety percent (90%) of ORTHO's United States requirements or seventy-five percent (75%) of ORTHO's worldwide requirements of Active Ingredients; provided, however, that ENZO shall have this right to supply and ORTHO shall have this obligation to purchase only with regard to Active Ingredients supplied to ORTHO at prices and time schedules which are reasonably competitive with those of other sources....	3. Pricing. The Compound shall be supplied to CEPHALON EXW LAFON's Manufacturing Facility in Maisons - Alfort, France, at the following prices: ... b) All quantities of the Compound other than those mentioned under (a) above shall be supplied at a price equal to eleven percent (11%) of CEPHALON's Net Sales of Licensed Products in the Territory, provided that if CEPHALON's finishing costs (including formulation, tabletting and packaging costs), exceed 3% of Net Sales, CEPHALON and LAFON shall meet to determine whether an adjustment in the price of the Compound under this Agreement is appropriate. ...

In this case, the Supply Agreement has *more* specific pricing than the *Enzo* agreement – a specific price of 11% of Net Sales, as opposed to *Enzo's* referral to less precise "reasonable times

and prices." *See* PTX-48 at CPH_PLD_23463.[7]

Other portions of the Supply Agreement confirm this is a sale. The Supply Agreement includes a Product Supply paragraph confirming Lafon is selling modafinil:

> 2. Product Supply
> [Lafon] will sell such Compound to CEPHALON, directly or through a designated seller, and CEPHALON will purchase from LAFON (or such designated seller) all such quantities of the Compound as CEPHALON (and its sublicensees) may require in order to make or have made the Licensed Products during the term of this Agreement.…

Id. at CPH_PLD_23463 (emphasis added); *see also id.* at CPH_PLD_23462, 2d Whereas Clause.[8]

Further, Lafon shipped Lot 003 API and Lot M006 tablets to Cephalon pursuant to the Supply Agreement in July 1993 before the critical date of October 6, 1993. 3/29 T. Tr. at 134:24-136:19 (Beach); PTX-66A at CPH_PLD_18869-70; Dkt. No. 438, Stipulations at ¶¶ 18-19. This shipment was an invalidating commercial sale because it was made in exchange for the consideration of Cephalon completing the clinical trials necessary to commercialize modafinil in the United States, even if the contract says "free of charge." PTX-48 at CPH_PLD_23463, ¶ 3(a) (linking "free" tablets to Cephalon's clinical trials, which Cephalon provided equally "free of charge" to Lafon); 4/5 T. Tr. at 124:3-125:1 (Grebow stating Cephalon's clinical trials cost millions of dollars); s*ee* U.C.C. § 2-304(1) ("The price can be made payable in money or otherwise. If it is payable in whole or in part in goods each party is a seller of the goods which he

[7] The definition of "Net Sales" and "Territory" is found in the License Agreement (PTX-49), which is properly referred to because "[a]ll capitalized terms not otherwise defined [in the Supply Agreement] shall be used as defined in the License Agreement." *See* PTX-48 at CPH_PLD_23462 (first sentence of "Definitions" section).

[8] In addition to defining pricing and supply, the Supply Agreement (PTX-48) includes numerous other provisions that evidence that this is a commercial contract for the sale of goods, namely modafinil tablets, including: Section 4, Estimates, which requires Cephalon to provide written estimates; Section 5, Invoices, which define the currency and timing of payment; Section 6, Shipping, which define when title passes from Lafon to Cephalon; Section 7, Warranties and Covenants; Section 8, Right of Rejection, which provides that if Cephalon does not reject a batch within thirty days, it is deemed to comply; and Section 12, Term, which provides that the contract takes effect on January 20, 1993 and remained in effect at all relevant times in this case.

is to transfer."); *Enzo*, 424 F.3d at 1283 (shipping an embodiment falling within the scope of the patent is sufficient to establish on-sale bar).[9]

The commercial nature of the Supply Agreement is further demonstrated by (1) the fact that Lafon engaged in a method of manufacturing modafinil "scaled up for commercial production" in early 1993 while negotiating the Supply Agreement (*see* JTX-1, at col. 5:1-5) and (2) Cephalon's actual payment of substantial money to Lafon for tablets under ¶ 3(b) of the Supply Agreement in subsequent years. *See* Dkt. No. 455, 1/27/04 Dep. Tr. at 25:8-12-26:25 (Heacock stating that Cephalon has paid for Lafon tablets since 1999 pursuant to the Supply Agreement). Under *Enzo*, the Supply Agreement (PTX-48) and/or the shipment of Lots 003 and M006 modafinil constitute a commercial sale (or at least an offer for sale) under the first prong of *Pfaff*.[10]

2. The sale was for modafinil falling within the scope of the claims.

While the Supply Agreement does not contain particle size specifications, that does not matter for the on-sale bar because "[i]t is well settled in the law that there is no requirement that a sales offer specifically identify all the characteristics of an invention offered for sale or the parties recognize the significance of all of these characteristics at the time of the offer." *Abbott*

---

[9] Under *Pfaff*, it is proper to look to the UCC to determine whether an offer for sale is made. At closing, Cephalon basically conceded that the shipment of 50,000 tablets was not in fact "free":

Court:	Do you really understand the deal to be that literal?
Mr. Gunther:	Your Honor –
Court:	Total gratuitous, here is 50,000 pills for free?
Mr. Gunther:	No. Your Honor, of course it was in the context of an entire agreement, there is no question about that. ...

4/7 T. Tr. at 30:2-9.

[10] Cephalon will likely cite *Elan*, but that case is readily distinguishable because there was no qualifying sale under the UCC as there was no signed agreement. *Elan Corp., PLC v. Andrx Pharms., Inc.*, 366 F.3d 1336 (Fed. Cir. 2004). The *Enzo* case is controlling because it involves a *signed* contract similar to the Supply Agreement. *See also Buildex*, 849 F.2d at 1464 (a contract fully satisfies the on-sale requirement).

Labs. v. Geneva Pharms., Inc., 182 F.3d 1315, 1319 (1999). Critically, all Apotex has to show is that Lafon sold one embodiment falling within the scope of the claims. *See Scaltech*, 269 F.3d at 1330 ("It is sufficient to show that one embodiment of the invention was offered for sale during the one-year period.") (emphasis added). If the one embodiment inherently possesses the limitations in the claims, then the invention is on sale, as established in *Abbott*:

> If a product that is offered for sale inherently possesses each of the limitations of the claims, then the invention is on sale, whether or not the parties to the transaction recognize that the product possesses the claimed characteristics.

182 F.3d at 1319.

Here, there is no dispute that Lafon Lot 003 API and Lot M006 100 mg tablets shipped pursuant to the Supply Agreement in July 1993 were products that meet the "95% less than 220 micron" and "median diameter" limitations of the claims. Dkt. No. 438, Stipulations, at ¶ 18-19; 3/29 T. Tr. at 58:16-59:5; 136:6-19 (Cephalon stipulating); 3/29 T. Tr. at 184:15-18 (Beach); 3/30 T. Tr. at 59:19-60:9 (Beach). Cephalon did not reject the July 1993 modafinil shipment as non-conforming goods, which confirm that small particle modafinil was on-sale under the Supply Agreement. *See* PTX-48 at CPH_PLD_23465-66; 3/29 T. Tr. at 147:17- 148:3 (Beach). This establishes the on-sale bar because *Pfaff* is satisfied as long as there is a sale of product meeting the claim limitations before the critical date, even if those goods were manufactured pursuant to an agreement that does not indicate whether the sold product will meet the claim limitations. *See Robotic Vision Sys., Inc. v. View Eng'g, Inc.*, 112 F.3d 1163, 1169 (Fed. Cir. 1997) ("[c]ompletion of the invention prior to the critical date, pursuant to an offer to sell that invention, would validate what had been theretofore an inchoate, but not yet established, bar"); *Enzo*, 424 F.3d at 1281-82 (finding on-sale bar where seller shipped an embodiment of the claimed invention pursuant to a contract that did not itself resolve the issue). Because these lots

were on sale, they are anticipatory under *Abbott* and *Scaltech* whether or not Lafon appreciated the particle size, dissolution rate, or bioavailability of these lots.

The Supply Agreement and/or the sale of Lot 003 API and Lot M006 100 mg tablets meet each of the limitations of the asserted claims of the '516 patent. The "pharmaceutical composition" claims (1-3, 7-9 and 13) were on sale because the Lafon Lots are embodiments of those claims falling directly in their scope, especially because the 100 mg tablets are solid oral dosage forms with an effective amount of modafinil within the claimed range. 3/29 T. Tr. at 137:4-138:21; 140:22-142:20 (Beach).[11] The "method of use" claims (4-6, 10-12 and 16) were also on-sale for purposes of § 102(b) because Lafon told Cephalon of modafinil's utility as an effective treatment for narcolepsy at daily doses of 200-400 mg.[12] *See Enzo*, 424 F.3d at 1285 (sale of probes falling within the scope of the claims and instructions how to use them in a hybridization assay was effectively an offer to sell the claimed assay methods); *Scaltech*, 269 F.3d at 1328 (a claim to a process was on sale when patentee offered to perform the claimed process before critical date).

C. Second *Pfaff* Prong: Lafon's Small Modafinil Tablets Were "Ready For Patenting"

The "ready for patenting" prong can be met by showing one of the following: (1) reduction to practice before the critical date; or (2) drawings or other descriptions of the invention had been prepared before the critical date that enable a person skilled in the art to

[11] Claim 13 is invalid because Lafon's manufacturing process allowed the M006 tablets to contain excess modafinil. *See* PTX-66B at AI89854; 3/29 T. Tr. at 115-118, 137-138:20 (Beach). Claim 14 is also invalid because it incorporates what was taught in the USP (PTX-26) as a way to formulate a product. 3/29 T. Tr. at 116:25-117:26; 178:8-25 (Beach); 4/5 T. Tr. at 146:8-19 (Grebow).

[12] Cephalon conceded that it knew that modafinil was effective for treating narcolepsy prior to its involvement with Lafon. 3/29 T. Tr. at 128:1-15 (Cephalon stipulating); 3/30 T. Tr. at 108:10-18 (Cephalon stipulating). This is further supported by documents and testimony. *See, e.g.*, 3/30 T. Tr. at 127:16-128:3 (Feifel); 3/31 T. Tr. at 81:24-82:6 (Palmieri); 4/4 T. Tr. at 119:22-120:4 (Baranski); PTX-17, PTX-27, PTX-31, PTX-43; PTX-64; PTX-64A.

practice the invention. *See Pfaff*, 525 U.S. at 67-68.[13]

In *Abbott*, two foreign companies manufactured drug compounds that fell within the scope of Abbott's patent claims and sold it before the critical date. 182 F.3d at 1318. However, at the time of the sale, the companies had no idea that they actually sold the specific crystalline form that was later claimed. *Id.* Still, the earlier unwitting sales were invalidating under § 102(b) because that crystal form was reduced to practice, i.e. actually manufactured, because "'[a] composition of matter is reduced to practice when it is completely composed.'" *Id.* quoting *Pfaff*, 525 U.S. at 57, n.2. Also, the product was "decidedly useful" because it was sold commercially. *Id.*

In this case, small particle modafinil sold by Lafon was ready for patenting because it was reduced to practice in the § 102(b) context as established by *Pfaff* and *Abbott*.[14] By the critical date, Lafon had already manufactured 315 pounds of Lot 5/2435 small particle modafinil API, determined its particle size, and used that to create one million (1,000,000) modafinil tablets. *See* PTX-83 at CPH-FTC 32140; PTX-184B at AI89846. Before the critical date, Lafon had additionally manufactured 467 pounds of Lot 003 small particle modafinil, determined its particle size, and used that to make an additional one million tablets. *See* PTX-83 at CPH-FTC 32136; PTX-184B at AI89846.[15]

There also can be no dispute that Lafon and others knew small particle modafinil was

[13] Notably, conception is not required to be ready for patenting. In *Abbott*, the patentee argued that there could be no on-sale bar because there was no conception. 182 F.3d at 1318. This was squarely rejected by the Federal Circuit, "[w]e disagree that proof of conception was required." *Id.*; *see also Scaltech*, 269 F.3d at 1331(rejecting Scaltech's argument that there can be no reduction to practice before it conceived of the claimed limitations.)

[14] Alternatively, the small particle modafinil was also ready for patenting because Lafon had established manufacturing procedures that were creating small particle modafinil and had "drawing or descriptions" of the particle size in the form of PTX-83. *See Pfaff*, 525 U.S. at 67-68

[15] In fact, Lafon manufactured even more small particle modafinil by October 6, 1993, in the form of lab-scale Lots 1/0103, 001 and commercial Lots 004 and 005. *See* PTX-83 at CPH-FTC 32134-35, 38-39.

useful for a number of independent reasons. First, like in *Abbott*, it was subject of the commercial sale to Cephalon established above, making it "decidedly useful." *See* 182 F.3d at 1318. Second, Apotex showed, and Cephalon repeatedly conceded, that it was well known that modafinil was safe and effective for the treatment of narcolepsy. *See supra* at n. 12. Cephalon even told the FDA in June 1993 that Lafon received approval from the French government to use modafinil to treat narcolepsy in humans in 1992. *See* PTX-64A at CPH_PLD_1869.[16] Cephalon cannot now claim that the modafinil Lafon actually manufactured, i.e. the small particle modafinil and tablets, was not useful. Third, Lafon actually used small particle modafinil (from Lot 5/2435) in French clinical trials, which were successful showing its utility as an effective treatment for narcolepsy. *See* 3/29 T. Tr. at 155:22-156:3; 161:9-16 (Beach); PTX-104 at CPH_PLD_71298; PTX-43; 3/30 T. Tr. at 107:8-108:9; 110:5-111:17; 113:11-115:6 (Feifel); PTX-95A; PTX-79; PTX-64 at CPH_PLD_1913-17; PTX-47; PTX-103. "The fact that the claimed material was sold under circumstances in which no question existed that it was useful means that it was reduced to practice." *Abbott*, 182 F.3d at 1318.[17]

D. There is no evidence of an experimental use that would negate the on-sale bar.

There are certain, narrow circumstances where an on-sale bar can be negated by what is referred to as the "experimental use" exception, but they do not apply here.[18] *See Clock Spring,*

[16] Lafon's small particle modafinil batches 5/2435, 001, 003, 004, and 005 all met Lafon's internal specifications which were the basis of their French approval (100% particles < 300 microns), and thus were expected to be effective for narcolepsy (i.e. useful).

[17] Because the '516 patent claims have no limitations to the alleged improved properties, Apotex does not need to establish that Lafon reduced to practice or even recognized a modafinil composition with those properties. Further, requiring a specific appreciation of certain qualities of the modafinil under the on-sale bar would be directly contrary to the holding in *Abbott* that "the parties' ignorance that they were dealing with Form IV is irrelevant." 182 F.3d at 1318; *see also Scaltech*, 269 F.3d at 1331.

[18] It should be noted that "the question posed by the experimental use doctrine, assessed under the first prong of the two-part on-sale bar test of *Pfaff*, is not whether the invention was under development, subject to testing, or otherwise still in its experimental stage at the time of the asserted sale." *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1354 (Fed. Cir. 2002) (emphasis added). "Commercial exploitation, if not incidental to the primary

L.P. v. Wrapmaster, Inc., 560 F.3d 1317, 1327 (Fed. Cir. 2009). First, the experimental use negation cannot apply because Lafon had already reduced to practice pharmaceutical compositions (i.e. tablets) made from small particle modafinil lots, such as Lots 5/2435 and 003, as discussed above. *See, e.g., Cargill, Inc. v. Canbra Foods, Ltd.*, 476 F.3d 1359, 1371 n.10 (Fed. Cir. 2007) ("Once the invention is reduced to practice, there can be no experimental use negation.").

A second, independent reason the experimental negation rule does not apply is that any commercial exploitation must be incidental to the experimentation. *Allen Eng'g*, 299 F.3d at 1354. As shown above, the Supply Agreement (PTX-48) had substantial commercial implications, including the requirements in Paragraph 3(b) that controlled millions of dollars in expected (and realized) sales. Further, arguments similar to Cephalon's expected arguments were considered and rejected by the Federal Circuit in *Enzo*. 424 F.3d at 1281-82 (a future requirements provision was sufficient to demonstrate a substantial commercial sale that precluded an experimental use negation, despite the contract also relating to experimental work).

A third, independent reason is that the experimental use exception only applies where "the claimed features or overall workability are being tested for purposes of the filing of a patent application." *Clock Spring*, 560 F.3d at 1327. Here, there is no evidence that either Lafon (the seller) or Cephalon entered into the Supply Agreement with a primary purpose of doing the clinical experiments to support any patent filing. *See, e.g.*, 4/5 T. Tr. at 74:15-75:1; 75:18-24 (Grebow explaining that Cephalon had not considered filing for a patent until mid-1994, a year and a half after the Supply Agreement was signed).

---

purpose of experimentation, will result in an on sale bar, even if the invention was still in its experimental stage." *Scaltech Inc. v. Rectec/Tetra LLC*, 178 F.3d 1378, 1384 n.1 (Fed. Cir. 1999). As such, that Cephalon conducted clinical trials with the Lafon tablets does not necessarily make it an "experimental use" for § 102(b) purposes.

IV. The Claims of the '516 Patent are Invalid Under 35 U.S.C. § 102(f) ("Derivation").

A. Legal Framework.

A patent is invalid for derivation under § 102(f) when the named inventors are not the true inventors of the claimed subject matter. *See* 35 U.S.C. § 102(f) (stating one is not entitled to a patent where "he did not himself invent the subject matter sought to be patented"). Under §102(f), one cannot reproduce or claim an invention created by someone else. *See OddzOn Prods., Inc. v. Just Toys, Inc.*, 122 F.3d 1396, 1401-02 (Fed. Cir. 1997) ("one cannot obtain a patent on that which is obtained from someone else whose possession of the subject matter is inherently 'prior.'"). Derivation under § 102(f) can be shown by proof of prior conception of the invention by another and communication by any means to the patentee. *See MacMillan v. Moffett*, 432 F.2d 1237, 1239 (C.C.P.A. 1970).[19]

B. Lafon scientists conceived of claimed small particle modafinil, at least as exemplified in Lots 5/2435 and 003.

Conception is the formation in the mind of the inventor of a definite and permanent idea of the complete and operative invention as it is hereafter to be applied in practice. *Solvay S.A. v. Honeywell Int'l, Inc.*, 622 F.3d 1367, 1377 (Fed. Cir. 2010). The '516 patent is for a pharmaceutical composition comprising small particle modafinil. Conception of a pharmaceutical composition merely requires knowledge of its structure, an operative method of making it, and, at most, an appreciation that the composition will have a utility. *See Burroughs Wellcome Co. v. Barr Laboratories, Inc.*, 40 F.3d 1223, 1229 (Fed. Cir. 1994) ("[c]onception of a chemical substance includes knowledge of both the specific chemical structure of the

[19] Because possession of an invention can also be proven by an actual reduction to practice, *see Pfaff*, 525 U.S. at 66 (an invention is "a concept that is complete" and "reduction to practice ordinarily provides the best evidence that an invention is complete"), proof of Lafon's actual reduction to practice (*supra* at Section III.C) coupled with communication to Cephalon can also prove derivation under § 102(f). *See also Ciric v. Flanigen*, 511 F.2d 1182, (C.C.P.A. 1975) (inventor was party who proved actual reduced invention to practice prior to other party's conception date).

compound and an operative method of making it."); 4/6 T. Tr. at 151:23-152:1 (Stoner admitting all that is required is conception of a substance that falls within the scope of the claim); *id*. at 156:10-17 (any pharmacological activity sufficient).

If one makes something, and knows they have made it, they have conception. *Dow Chem. Co. v. Astro-Valcour, Inc.*, 267 F.3d 1334, 1341 (Fed. Cir. 2001) ("[T]he cases establish that the date of the conception of a prior inventor's invention is the date the inventor first appreciated the fact of what he made"). Apotex does not have to show that Lafon appreciated the "95% less than 220 micron" language that Cephalon later chose to use in its patent claims. *See Teva Pharm. Indus. Ltd. v. AstraZeneca Pharms. LP*, 08-cv-4786, 2010 U.S. Dist. Lexis 112597 (E. D. Pa. October 20, 2010) (J. Yohn) at *37 (an "inventor must establish that he recognized and appreciated a compound corresponding to the compound defined by the claims.") (emphasis added). Nor does it have to show that Lafon thought that the small particle modafinil was patentable. *Dow*, 267 F.3d at 1341. It is sufficient to show that Lafon knew the particle size of what it made because that is all that is claimed.

Critically, there is no need to show Lafon conceived of or appreciated Cephalon's alleged unexpected benefits, such as consistent dissolution, for the '516 patent to be invalidated under § 102. *See MacMillan*, 432 F.2d at 1239 ("We do not think that the conceiver must know the unexpected properties associated with the conceived invention, nor even that the conceived subject matter is new."); *In re Wiggins*, 488 F.2d at 543 (unexpected results irrelevant to anticipation); 4/6 T. Tr. at 148:1-149:2 (Stoner so admitting, including that "the information in the Shek declaration, even if it's totally unexpected, could not overcome a 102 rejection").

Apotex established, and Cephalon conceded, that Lafon scientists, independent of Cephalon, manufactured Lots 5/2435 and 003 by January 1993, as described above. Apotex

established, and it was conceded, that Lafon scientists independent of Cephalon measured the particle size of Lot 5/2435 and Lot 003 by January 1993. There can be no reasonable dispute that Lafon scientists knew that Lot 5/2435 and Lot 003 had a pharmacological activity – Lafon made 1,000,000 tablets from Lot 5/2435 and successfully used them in numerous clinical trials, and Lot 003 has a similar particle size distribution.[20] *See supra* at Section III(C). In sum, Lafon scientists conceived of small particle modafinil because they independently manufactured it, measured its particle size, and demonstrated it had a use in the treatment of narcolepsy and other conditions. *See Teva*, 2010 U.S. Dist. Lexis 112597, at *16 (finding AstraZeneca conceived of the invention because they knew and conceived of a stable composition with a specific ingredient, which fell within the scope of the claims, even though they did not believe or appreciate that the ingredient caused the stability). Even Mr. Michel Moisan, a Cephalon France (previously Lafon) employee, said that he was surprised that "Cephalon had patented the particle size of our [Lafon's] product" because if it was supposed to be done, Lafon could have done it because it was the owner of the molecule and Cephalon was their client. Dkt. No. 455, 4/1/04 Dep. Tr. at 171:7-172:4 (Moisan).[21]

C. Lafon scientists communicated small particle modafinil, at least as exemplified in Lots 5/2435 and 003.

[20] Even if one assumes Cephalon helped to confirm that small particle modafinil was effective (it did not – Lafon had already used small in clinical trials), Lafon scientists were still the original inventors of the modafinil they independently created and measured the particle size of. *See MacMillan*, 432 F.2d at 1238 (holding that MacMillan, who ran tests that proved the effectiveness of the claimed compound, derived the invention from Moffett, who selected and sent the compound and 68 others for testing, and declaring Moffett the proper inventor).

[21] The deposition testimony of the "Lafon" scientists (Nguyen, Leyder, Moachon, Moisan) regarding the discovery of the "improved' properties of modafinil at the alleged 220 micron threshold should be given minimal, if any, weight. First, these witnesses were Cephalon employees at the time of their depositions. *Cf.* Dkt. No. 438, Stipulations, at ¶ 13 (Cephalon purchased Lafon in 2001). Further, these "improved" properties are irrelevant to derivation (and on-sale bar) because they are not claimed, as described above in Section I. Finally, this testimony is contradicted by earlier, contemporaneous documents. *See, e.g.*, PTX-20A (improved dissolution), PTX-56 (relationship between particle size, bioavailability and dissolution rate), and PTX-73A (particle size causing bioavailability differences).

The communication of this invention occurred no later than July 23, 1993, when Lafon sent Cephalon small particle modafinil API and 100 mg tablets after earlier providing instructions to use 200-400 mg/day for the safe and effective treatment of narcolepsy. *See* Dkt. No. 438, Stipulations at ¶ 19; PTX-66A; PTX-56 at CPH_PLD_18795; 4/6 T. Tr. at 117:9-20 (Grebow admitting Lot 003 sent to Cephalon was GMP compliant). This communication is sufficient because it enables one to practice the claimed invention. *See Hedgewick v. Akers*, 497 F.2d 905, 908 (C.C.P.A. 1974) ("Communication of a complete conception must be sufficient to enable one of ordinary skill in the art to construct and successfully operate the invention."); 4/5 T. Tr. at 122:17-21 (Grebow admitting anyone with the capability to measure particle size would be able to readily determine the particle size of the modafinil API sent to him).[22] Additional communication verifying the particle size of the modafinil delivered in July 1993 modafinil was received by Cephalon by November 15, 1993 (*see* PTX-83), which is before Dr. Grebow claimed to have conceived of the "95% less than 220 micron" limitation.[23,24]

D. Cephalon's expected arguments are without merit.

Cephalon may argue that Lafon's manufacture of small particle modafinil was accidental

[22] Dr. Grebow was at most, if not all, of the meetings between Lafon and Cephalon that discussed modafinil, its particle size, the impact of particle size, and the fact that it was clinically safe and effective in the treatment of narcolepsy. *See, e.g.*, PTX-37; PTX-56; PTX-57. Clearly, he knew that the modafinil provided was intended for the treatment of narcolepsy. *See MacMillan*, 432 F.2d at 1239-40 (finding a communication of a complete conception when inventor sent compound, which was later claimed, to deriver in light of deriver's prior understanding of utility from parties' prior dealings).

[23] Cephalon did not present evidence explicitly establishing a date Dr. Grebow and the other inventors conceived of either the invention actually claimed in the '516 patent or the "220 micron threshold yields improved properties" invention that they have asserted at trial. However, it is clear that the first time the Cephalon patentees thought of modafinil particle size was sometime after their U.S. clinical trial was halted on October 4, 1993.

[24] Dr. Grebow admitted that Cephalon wrote the 95%< 220 micron internal specification around the Lot 003 modafinil received from Lafon. 4/5 T. Tr. at 64:5-11 (Grebow). The only document identified by Dr. Grebow with the 220 micron specification was from after the filing of the '516 patent application, in October 1994. 4/5 T. Tr. at 135:24-136:6 (Grebow); PTX-207 (10/19/94 memo recommending in-house specifications); *cf.* JTX-4 at CPH_PLD_465-67 (Burgoon declaration to shown invention before Sep. 29, 1994). Furthermore, Dr. Heacock, who is not a named inventor, testified that he, and not Dr. Grebow, was the one who first proposed the 95%<220 specification. *See* Dkt. No. 455, 1/29/04 Dep. Tr. at 64:10-66:20 (Heacock), which further demonstrates that Cephalon did not consider this supposed "threshold" its invention (otherwise Heacock would be an inventor).

or unintended. First, this argument is factually not supportable because all six non-recrystallized batches of modafinil Lafon manufactured from January 1989 through July 1993 were small. 3/29 T. Tr. at 162:17-163:2 (Beach stating that, in his experience, the trend in Lafon's data does not happen by accident); PDX-2 summarizing PTX-83; Dkt. No. 455, 3/30/04 Dep. Tr. 81:14-25 (Leyder stating particle size decreased as part of the natural evolution of, and was inherent in, Lafon's production). The odds of that happening by chance alone are very small.[25] Further, small particle modafinil could not be an accident because Lafon scientists considered Lot 003 their GMP lot and "current standard product" on June 23, 1993. *See* PTX-63B.

Second, even if one could argue the production of six lots of small modafinil was accidental, the small particle size was no longer unappreciated once Lafon scientists measured the particle size of these lots in April-May 1993. See PTX-83. The "lack of appreciation" cases only apply in certain, limited circumstances where the first party did not determine something existed or measure the parameter required until after the conception date of the other party. For example, in *Heard v. Burton*, Mr. Heard "did not at the time know or identify the alumina as eta-type," which could only be determined by X-ray diffraction – a test Heard did not perform in time. 333 F.2d 239, 241 (C.C.P.A. 1964); *see also Langer v. Kaufman*, 465 F.2d 915, 918-19 (C.C.P.A 1972) (party did not even know it had a certain form of the compound); *Invitrogen Corp. v. Clontech Labs.*, 429 F.3d 1052, 1067 (Fed. Cir. 2005) (claim explicitly required "no RNase H activity" for mutant reverse transcriptase when purported inventor had not tested for that before the required date); *cf. Cooper v. Goldfarb*, 240 F.3d 1378, 1385 (Fed. Cir. 2001) (If Cooper knew the fibril lengths of the material he sent to Goldfarb, "then he could establish

[25] As was remarked in closing, Lafon was "batting a thousand" in manufacturing small particle modafinil for its normal lots from 1989 through July, 1993. 4/7 T. Tr. at 69:22-70:25 (Breisblatt). In another way of looking at it, the odds that one would get small particle modafinil (as opposed to large particle modafinil) six times in a row by chance alone would be 1/64 or 1.6%.

reduction to practice."). Here, Lafon scientists knew they had modafinil and knew its particle size because they measured the lots they were producing, knew that Lot 5/2435 was small and effective, and specifically considered Lot 003 to be Lafon's standard product, all by June 1993, which is well before October 1993, which is the earliest possible conception date that Cephalon can claim.[26]

Cephalon may also argue Apotex did not identify a specific Lafon scientist as inventor. First, in cases of derivation (as opposed to priority disputes where the other party is also seeking a patent), identification of a specific person(s) should not be required. The patent statute establishes invalidity where the named inventors "did not themselves invent the subject matter." 35 U.S.C. § 102(f). Cephalon is not entitled to a patent because it did not invent anything. Cephalon took what it was given from Lafon and did nothing to modify or improve modafinil. *See, e.g.,* 4/5 T. Tr. at 134:20-135:19 (Grebow); Dkt. No. 455, 8/5/04 Dep. Tr. at 196:18-197:2, 250:13-251:3 (Shek); 4/7 T. Tr. at 33:7-25 (Cephalon admitting they did nothing to Lafon's product). Ultimately, Cephalon just requested that in the future, Lafon provide the same modafinil that it was already consistently manufacturing by July 1993. 4/5 T. Tr. at 64:5-11 (Grebow); Dkt. No. 455, 8/5/04 Dep. Tr. at 250:16-251:3 (Shek stating Cephalon just decided to use "a specific section of particle size and asked Lafon to reproduce what they did in the first batch to the United States to do the studies here. We didn't improve. We used the material. We didn't change a synthesis. That was their responsibility."). At most, Cephalon made a further discovery related to inherent properties of Lafon's small particle modafinil (*see* Dkt. No. 455, 8/5/04 Dep. Tr. at 22:18-23:3 (Shek)), but that is not sufficient to be considered an inventor. *See Solvay*, 622 F.3d at 1377-78; *In re Crish*, 393 F.3d 1253, 1258 (Fed. Cir. 2004) ("[J]ust as the

[26] Again, even if there are unexpected properties associated with the small particle modafinil Lafon created, Lafon did not have to appreciate them for conception. *MacMillan*, 432 F.2d at 1239.

discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.").

Second, other cases involving derivation issues did not require specific identification of the true inventor. For example, in *OddzOn*, the Federal Circuit considered confidential drawings prior art when they were given to the patentee without identifying the author of those drawings. *See OddzOn*, 122 F.3d at 1401-02.; *see also Solvay*, 622 F.3d 1367, 1377-78 (finding that Honeywell scientists derived the claimed method from unspecified "Russian engineers" and were not inventors of that method even though they were the first to do the method in the U.S.). As another example, the Federal Circuit's predecessor court affirmed a PTO finding of derivation under § 102(f) where a letter sent to the named inventor by an agent for a third party evidenced conception of what was claimed, even though there was no testimony by the author that he appreciated precisely what was written in the letter. *Applegate v. Scherer*, 332 F.2d 571, 573-74 (C.C.P.A. 1964). Under Cephalon's application of the law, one could replicate exactly what is fully described in an *anonymous* letter and obtain a patent because no specific person could be identified as the other inventor under § 102(f). That is not and cannot be the law.

Third, the evidence presented at trial establishes a number of Lafon employees could be considered co-inventors of the claimed modafinil. For example, Ms. Ducastel, head of Lafon's Analytical Department, authored a memorandum that appreciates that Lot 003 is Lafon's GMP and "current standard product." PTX-63B. She also discussed the correlation between particle size and dissolution profile at March 1993 meeting. PTX-56.[27] Ms. Ducastel was also working

[27] She is also an author of the Chemical, Pharmaceutical and Biological Documentation, which teaches that reduction of the particle size of modafinil results in increased dissolution. PTX-20A at CPH-FTC 45308, 326-27. It is reasonable to assume that she was aware that such modafinil was useful to treat narcolepsy, given that she worked at the company that developed modafinil, was present at meetings discussing that utility, and that she was asked to create a commercial GMP lot. *See MacMillan*, 432 F.2d at 796-797 (allowing for reasonable conclusion that a scientist would be aware of his own company's successful prior use).

with others in the Lafon modafinil team who were sharing knowledge about modafinil, its particle size, and the impact of particle size. *See, e.g.*, PTX-56 (meeting minutes identifying Lafon employees); PTX-83 (identifying M. Broquaire, Ms. Nadaud, and cc'ing Mr. Lafon and Dr. Laurent as being aware of the particle size of each batch). Further, the testimony of the Lafon employees established that Lafon was aware of the particle size of modafinil it produced, and does not dispute that Lafon scientists knew that it was effective for narcolepsy, i.e. had a utility. *See, e.g.*, Dkt. No. 455, 3/31/04 Dep. Tr. at 68:2-69:13 (Nguyen); 5/26/04 Dep. Tr. at 71:21-72:21 (Moachon). Further, by October 20, 1993, Mr. Moachon communicated to Cephalon patentee Dr. Stong that, in his opinion, particle size was responsible for any bioavailability difference seen in the US and foreign trials. *See* PTX-73A at CPH-FTC 23247 ("... in my opinion, the tablets used by Lafon have a different bioavailability than these used by CEPHALON ... This difference is due to difference in particle size ....") (emphasis added).[28] As such, Lafon scientists were inventors of the claimed modafinil compositions and methods of the '516 patent.

V. The Claims of the '516 Patent are Unenforceable Due to Inequitable Conduct

A. Legal Framework

Patent applicants and their attorneys "are required to prosecute patent applications with candor, good faith, and honesty." *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc*, 326 F.3d 1226, 1233 (Fed. Cir. 2003); *see also* 37 C.F.R. § 1.56(a), (c).[29] Further, all patent practitioners know of their duty of candor because it is part of the test to become licensed before the PTO. 4/6 T. Tr. at 149:3-24 (Stoner); Dkt. No. 455, 10/27/2010 Dep. Tr. at 15:17-16:20,

[28] Cephalon has not established a conception date prior to this date. *See supra* at n. 23 and 24.

[29] Cephalon's in-house counsel Mr. Richard Burgoon, outside counsel Mr. Paul Clark and Mr. Gary Creason, and the named inventors all had a duty of candor in relation to the '845 and '516 patent applications. *See* 4/1 T. Tr. at 139:10-140:2 (Gerstman); *see also* 37 C.F.R. § 1.56(c).

129:7-130:10 (Burgoon). The duty of candor is especially important for confidential pieces of prior art, like some on-sale bars and derivation, because the PTO cannot find out about them through the its search tools or otherwise.[30] *See id.* at 149:25-150:3 (Stoner stating that the duty of candor applies to confidential material information). Patent practioners know that if they have confidential material information (like a Supply Agreement), they either have to disclose the information or not not seek patent claims. *Id.* at 150:4-151:6 (Stoner); *see also* 4/1 T. Tr. at 127:24-128:3 (Gerstman).

Inequitable conduct is established by proof of two elements: (1) a failure to disclose known material information, an affirmative misrepresentation of material fact, or submission of materially false information to the PTO ("materiality"), and (2) intent to mislead or deceive the PTO ("intent"). *See Cargill*, 476 F.3d at 1363-64.[31] A threshold level of both materiality and intent must be shown. *Praxair, Inc. v. ATMI, Inc.*, 543 F.3d 1306, 1313 (Fed. Cir. 2008).

The materiality element is met where those involved in the prosecution are aware of information that a reasonable examiner would "likely consider important in deciding whether to allow an application to issue as a patent." *Cargill*, 476 F.3d at 1364 (internal quotation omitted).[32] "Materiality is not limited to prior art but embraces *any* information that a reasonable examiner would be substantially likely to consider important in deciding whether to allow an application to issue as a patent." *Bristol-Myers*, 326 F.3d at 1325 (italics in original). Potential on-sale bars and inventorship/derivation issues are material. *Atlanta Attachment Co. v. Leggett*

[30] In this case, Apotex's evidence of invalidating on-sale bar and derivation was not before the PTO. 4/6 T. Tr. at 151:3-6 (Stoner).

[31] Some cases separate the materiality factor into showing (1) that material information exists and (2) the applicant or his or her attorney knew of this information and that it was material. *See Brasseler, USA I, LP v. Stryker Sales Corp.*, 267 F.3d 1370, 1375 (Fed. Cir. 2001).

[32] Materiality is further defined in 37 C.F.R. § 1.56(b). *See Cargill*, 476 F.3d at 1364 (§ 1.56(b) does not supplant reasonable examiner standard, both can be used to determine materiality).

& Platt, Inc., 516 F.3d 1361, 1368 (Fed. Cir. 2008); *Brasseler*, 267 F.3d at 1381-86; *Adv. Magnetic Closures, Inc. v. Rome Fastener Corp.*, 607 F.3d 817, 830 (Fed. Cir. 2010).

The word "potential" is used because information is material even if it ultimately would not invalidate the claim. *See Cargill*, 476 F.3d at 1367. Even if those prosecuting the patent think that information is not invalidating, "[c]lose cases should be resolved by disclosure, not unilaterally by the applicant." *Id.* (citation omitted); 4/6 T. Tr. at 164:30-165:6 (Stoner stating that MPEP teaches to err on the side of caution [i.e. disclosure]).[33]

For the intent inquiry, patent applicants rarely admit directly to committing inequitable conduct. *Merck & Co., Inc. v. Danbury Pharmacal, Inc.*, 873 F.2d 1418, 1422 (Fed.Cir.1989) ("Intent need not, and rarely can, be proven by direct evidence."). As such, an intent to deceive is usually inferred from the facts and circumstances surrounding the conduct at issue. *Cargill*, 476 F.3d at 1364 (internal citations omitted); *see also Adv. Magnetic Closures*, 607 F.3d at 830 (affirming district court finding of intent where "the single most reasonable inference able to be drawn from the evidence" was intent to deceive).

After the accused infringer has made threshold showings of materiality and intent, the Court must then balance the levels of materiality and intent to determine whether the conduct at issue amounts to inequitable conduct. *Cargill*, 476 F.3d at 1364. Under the balancing test, the more material the omission or the misrepresentation, the lower the level of intent required to establish inequitable conduct. *Bristol-Myers*, 326 F.3d at 1234 ("[W]hen balanced against high materiality, the showing of intent can be proportionally less."). If on balance the applicants committed inequitable conduct, the patent is unenforceable. *Cargill*, 476 F.3d at 1364.

[33] *See* MPEP § 2004 ¶ 11 (PTX-142 at CPH-FTC 18921) ("[i]t may be desirable to submit information about prior uses and sales even if it appears that they may have been experimental, not involve the specifically claimed invention, or not encompass a completed invention.").

B. Those involved in the prosecution of the '516 patent[34] committed inequitable conduct.

The defining act of inequitable conduct in this case was the Cephalon applicants' decision to not tell the PTO about Lafon's role in the modafinil that formed the basis of all the asserted claims of the '516 patent: Lafon Lot 003 (referred to as Late Lot L-1 in the patent).[35] Lafon scientists independently manufactured Lot 003, measured the particle size of Lot 003, considered Lot 003 its standard product, and sold Lot 003 to Cephalon pursuant to the Supply Agreement, all while advising Cephalon to use 200-400mg/day for the safe and effective treatment of narcolepsy. *See supra* at Section III(B). As such, Lot 003 is prior art. Even Cephalon's patent law expert admitted that, if it is prior art, Lot 003 is material. 4/6 T. Tr. at 147:7-9 (Stoner). In fact, it is of the highest materiality because Lot 003 anticipates the claims as described above. *Id.* at 146:2-22 (Stoner admitting an example falling within scope of claims anticipates the claims). The Supply Agreement itself was never provided to the PTO and was also highly material, as it is an on-sale bar as demonstrated above.

There is also no dispute that those with a duty of candor, including Mr. Burgoon and Dr. Grebow, were aware that Lafon was the independent creator of Lafon Lot 003. 4/5 T. Tr. at 102-105; 107:13-25; 117:9-20; 134:20-135:18 (Grebow); Dkt. No. 455, 7/23/04 Dep. Tr. at 159:21-23 (Burgoon). Further, both Mr. Burgoon and Dr. Grebow knew that Lafon measured and knew the particle size of Lot 003. *See* PTX-83 (Nadaud letter sent to Grebow showing Lafon's particle size measurements); PTX-91 (Burgoon thanking Leusner for "reanalyzing" modafinil lots so that Cephalon "would not have to rely upon the particle size data provided to us by Lafon."). They

[34] In this section, Apotex's reference to the '516 patent and its prosecution includes prosecution of the '845 patent (JTX-4) and the reissue '516 patent (JTX-3).

[35] Lafon also produced, measured the particle size, and provided Cephalon with the other Late Lot (L-2) described and claimed in the '516 patent specification.

were both also aware of the Supply Agreement. 4/4 T. Tr. at 183:9-21 (Grebow); Dkt. No. 455, 7/23/04 Dep. Tr. at 159:21-23 (Burgoon). Dr. Grebow was also aware of the substantial amount of work done by Lafon on modafinil, including information linking the particle size of modafinil to dissolution and bioavailability. *See, e.g.,* PTX-56 at CPH_PLD_18794 ("The correlation between dissolution profile and particle size is also discussed.").

No one at Cephalon did anything to the Lot 003 tablets and API they received from Lafon – nothing to modify, change, improve or enhance them. *See* 4/5 T. Tr. at 134:20-135:18 (Grebow); Dkt. No. 455, 8/5/04 Dep. Tr. at 196:18-197:2, 250:13-251:3 (Shek). Yet the Cephalon applicants sought a patent that covers (and gives Cephalon a monopoly over) the exact Lot 003 modafinil they received from Lafon while purposefully choosing not to disclose that information. *See* PTX-91 (Burgoon writing "Without the efforts of this 'team' an opportunity which provides significant benefits to Cephlaon would have been lost ...."); Dkt. No. 455, 10/27/10 Dep. Tr. at 237:6-238:19 (Burgoon); 8/18/2004 Dep. Tr. at 80:3-7, 16-24; 82:16-83:11 (Creason admitting Claim 1 is for a composition of matter, but none of the named inventors invented a composition of matter).

If Dr. Grebow or Mr. Burgoon had told the PTO that Cephalon had signed agreements with Lafon under which it received Lafon's modafinil and information (including one of the lots that Cephalon was using as an embodiment of the invention) prior to October 1993, Cephalon would not have obtained the patent in issue. Just on the failure to inform the PTO of the Supply Agrement or Lafon's role in developing, manufacturing, and providing Lot 003, Cephalon's knowing omissions rise to the level of inequitable conduct.

However, there is more to show the intentional nature of these omissions. Cephalon wanted to be able to tell the PTO that it was the inventor of small particle modafinil. To do that,

it needed a story, and the story it chose to tell the PTO in the '516 patent application was that Lafon was only using large particle modafinil in foreign trials, and that Cephalon "discovered" small particle modafinil during the U.S. clinical trials. *See* JTX-1 at col. 4:54-67 (stating that the modafinil used in foreign clinical trials, i.e. the Early Lots, E-A through E-D, was large); *id.* at col. 5 (alleging discovery during U.S. clinical trials).

However, the documentary evidence in this case show that the premise of Cephalon's story was false. Dr. Grebow and his team learned the particle size of the different lots that Lafon has been manufacturing and measuring since 1986, prior to filing the '516 patent application. *See* PTX-83 (addressed to Grebow), summarized in PDX-2. As can readily be seen from PDX-2, Lafon had been manufacturing small particle modafinil for years before October 1994. Specifically, as described above, Lot 5/2435 was small and was manufactured into a million tablets that were used by Lafon in several successful "foreign" clinical trials.

Cephalon had to selectively disclose only large particle modafinil (including Lot 002A, which was never used in foreign clinical trials), while hiding from the PTO the existence of Lot 5/2435 small particle modafinil (even though it was used in the foreign clinical trials).[36] Neither Dr. Grebow, the other Cephalon "inventors," nor Mr. Burgoon ever told the PTO about Lot 5/2435, its particle size, or its use in foreign clinical trials. But Cephalon repeatedly made arguments on the patentability of small modafinil based on its false statement to the PTO that the foreign trials only used large particle modafinil. *See* JTX-1 at col. 4: 54-67; JTX-4 at CPH_PLD_253 (Cephalon's submission arguing "comparing small modafinil particles of the invention with the large particles of the prior art demonstrate unexpected superior properties of

[36] Cephalon may argue they only disclosed the Early Lots they chose to "re-analyze" the particle size of, but this would only confirm that they purposefully chose not to compare the small particle modafinil Dr. Grebow and others knew Lafon was using abroad in clinical studies, and does not excuse their telling the PTO the foreign trials used large particle modafinil when they knew they also used small modafinil.

the claimed modafinil"); Dkt. No. 455, 10/27/2010 Dep. Tr. at 257:24-260:12; 268:2-17; 273:7-11; 280:7-282:8 (Burgoon).[37] Cephalon's selective disclosure of only the large particle modafinil, coupled with its repeated arguments for patentability while withholding the information on Lafon's earlier small particle lots, is strong evidence of both intent and materiality.

Furthermore, the PTO considered the Early Lots that were disclosed (E-A through E-D) to be prior art to the '516 patent. JTX-4 at CPH_PLD_247 ("admitted prior art modafinil" ... "whose larger particle size ...."); *id*. at CPH_PLD_253 (Cephalon' response referring to "large particles of the prior art"). Critically, that means that if Cephalon had properly disclosed Lot 5/2435, the PTO examiner would have considered it prior art. *See Springs Window Fashions LP v. Novo Indus., L.P.*, 323 F.3d 989, 995-96 (Fed. Cir. 2003) (statements made by patentees in the specification or prosecution history of the patent are considered binding admissions that constitute valid prior art). If Cephalon properly disclosed 5/2435 like the other early lots, the claims would have been rejected as anticipated because that lot falls within the scope of the claim. Any reasonable examiner would want to know about invalidating prior art. As such, Lot 5/2435 would be of the highest materiality.

During prosecution, Cephalon repeatedly stated (including through sworn declarations) that a person of ordinary skill would not have been motivated to decrease the particle size of the prior art large particle modafinil because it was bioavailable and working in the foreign trials.[38] *See, e.g.,* JTX-4 at CPH_PLD_257; CPH_PLD_260; CPH_PLD_317; CPH_PLD_335,

[37] *See also* JTX-4 at CPH_PLD_333; *id.* at CPH_PLD_401 ("The same cannot be said ... for modafinil falling outside the scope of the claims."); *id.* at CPH_PLD_427 ("...modafinil ... having a particle size and distribution falling outside the scope of the present claims, had been clinically investigated in humans in studies outside of the United States ....").

[38] Cephalon continues to argue this point to refute Apotex's obviousness claim as discussed below.

CPH_PLD_343; CPH_PLD_348-49. This argument could not have been more misleading because (1) Lafon had already shown that small particle modafinil (Lot 5/2435) was bioavailable, safe, and effective in foreign clinical studies, *see supra* at Section III(C), and (2) Cephalon scientists did not modify anything; they simply used what was received from Lafon with no alteration.[39] *See, e.g.,* 4/5 T. Tr at 112:2-8, 135:3-11 (Grebow stating 5/2435 was being used in the treatment of narcolepsy and that Cephalon did not modify the modafinil); Dkt. No. 455, 8/5/04 Dep. Tr. at 250:13-15 (Shek stating Cephalon did not improve the modafinil it received from Lafon).[40]

The most damning piece of evidence of the intent to deceive the PTO is the internal memo from Mr. Burgoon to the inventors and executives at Cephalon. PTX-91. This self-congratulatory memo is the closest one can come to a confession in a patent case. It definitively shows that Lafon had previously accomplished everything that Cephalon ends up claiming as its invention and that Mr. Burgoon (as well as the inventors) made a purposeful decision to hide it from the PTO. *See* PTX-91 (thanking Leusner for reanalyzing modafinil lots so that Cephalon "would not have to rely upon the particle size data provided to us by Lafon."); ("this application is 'unusual' in the sense that we did not want to include any of Lafon's data so as to avoid disclosing their 'confidential' information; thus, the task of 'disclosure' of the invention was unique.") (single quotation marks in original). Mr. Burgoon even explains his motive for deceiving the PTO: "Without the efforts of this 'team' an opportunity which may provide

[39] This is in direct contrast to Cephalon's affirmative misrepresentation to the PTO that modafinil "had long been known, but had never before been modified as the inventors had done ...." JTX-4 at CPH_PLD_343 (emphasis added); Dkt. No. 455, 12/21/04 Dep. Tr. 204:24-205:13; 207:20-208:9 (Clark).

[40] Cephalon made additional misleading statements, which may not rise to the level of materiality, but provide additional evidence that Cephalon was intentionally misleading the PTO. For example, Cephalon presented the dog bioavailability study to the PTO in a way to emphasize differences between particle sizes, while presenting the same data to the FDA to show no differences. 3/30 T. Tr. at 132:9-134:1 (Feifel).

significant benefits to Cephalon would have been lost ...." *Id.* (emphasis added). The benefits of this patent were especially important to Cephalon because it was a small company with large investments in very few projects and no drugs on the market to bolster its losses. *See* 4/4 T. Tr. at 168:25-169:15; Dkt. No. 455, 6/8/07 Dep. Tr. 18:5-18, 42:1-9 (Baldino).[41]

Overall, the evidence demonstrates that Cephalon withheld highly material information (*e.g.*, the Supply Agreement, Lafon's role in Late Lots, Lot 5/2435) and made highly material affirmative misrepresentations (about modafinil used in foreign clinical trials) with an intent to deceive the PTO as demonstrated by the circumstantial and direct (PTX-91) evidence. This overwhelming evidence of both materiality and intent requires no balancing. This Court should find the '516 patent unenforceable, following the precedent where the Federal Circuit found inequitable conduct based on similar acts and evidence. *See Cargill,* 476 F.3d at 1365-68; *Merck*, 873 F.2d 1420-21; *Bristol-Myers*, 326 F.3d at 1233-42; *Brasseler*, 267 F.3d at 1375-80.

C. The Evidence Does Not Support Any Reasonable Excuse For The Acts Outlined Above.

Cephalon has failed to provide any plausible excuse for its failure to provide the information that only it possessed to the PTO. *See Brasseler*, 267 F.3d at 1381-82.[42] Also, there really can be no explanation for making false and misleading statements.

If Cephalon attempts to argue that Mr. Burgoon or Dr. Grebow failed to disclose information due to "confidentiality concerns," it should fail. Given that all patent practitioners know that the duty of candor applies to confidential information, that is not a reasonable excuse

[41] Also, Mr. Burgoon received significant pressure to secure the patent from Cephalon's CEO, Frank Baldino. For example, Dr. Baldino told Mr. Burgoon, "Rick, I know you'll get the '845 Patent to issue." Dkt. No. 455, 10/27/10 Dep. Tr. at 94:20-25 (Burgoon); *see also* PTX-112. At his 2010 deposition, Mr. Burgoon testified that he "can remember [the comment] like it was yesterday." Dkt. No. 455, 10/27/10 Dep. Tr. at 165:17-22 (Burgoon). Clearly, Dr. Baldino's message had an impact on Mr. Burgoon.

[42] At the very least, Mr. Burgoon, Dr. Grebow, and others at Cephalon should have known this was a close call and provided it to the PTO to let it make the decision. *See Cargill*, 476 F.3d at 1367.

sufficient to overcome the more reasonable inference of intent to deceive based on the evidence above. *See Brasseler*, 267 F.3d at 1381-82. Also, Cephalon's argument is not supported by circumstantial evidence as Cephalon presented nothing to show they made an effort to disclose the relevant information in a non-confidential way (e.g. disclosing that the claimed modafinil was independently created by a third party) or that they asked Lafon if it was acceptable to disclose the information. Further, Cephalon was allowed under the License Agreement to give necessary information to government agencies. *See* PTX-49 at CPH_PLD_23439.

Cephalon may also argue that the inequitable conduct should be excused because the applicants thought the invention was the alleged improved properties below the "220 micron threshold." Given the well-known principle that an embodiment falling within a claimed range anticipates the range (which Mr. Burgoon knew or should have known about), and Mr. Burgoon and Dr. Grebow's knowledge of Lafon's manufacture of Lots 5/2435 and 003, and the shipment pursuant to the Supply Agreemenet of Lot 003, which fall within the scope of what Cephalon was claiming, this excuse is also not reasonable. As such, the single most reasonable inference from all of the evidence discussed above demonstrates that the Cephalon applicants intended to deceive the PTO by withholding highly material information and making material misrepresentations.

VI. The Claims of the '516 Patent are Invalid Under 35 U.S.C. § 103(a) ("Obviousness").

A. Legal Framework.

A patent is invalid under 35 U.S.C. § 103(a) when "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." Obviousness is a legal conclusion based on four factual

inquiries: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any secondary considerations such as unexpected results or commercial success. *See KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 406 (2007).[43] Obviousness is established where "a person of ordinary skill in the art would have had reason to attempt to make the claimed composition ..., or carry out the claimed process, and would have had a reasonable expectation of success in doing so." *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007).[44]

B. The Person of Ordinary Skill in the Art Related to the '516 Patent Claims.

"The issue of obviousness is determined entirely with reference to a hypothetical 'person having ordinary skill in the art.' The actual inventor's skill is irrelevant to the [obviousness] inquiry ...." *Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985); "A person of ordinary skill is also a person of ordinary creativity, not an automaton." *KSR*, 550 U.S. at 421. A person of ordinary skill related to the '516 patent would likely have a Ph.D. in pharmaceutical sciences or a related field and have three or more years of practical experience and an appreciation of the fields involved in the development of a commercial pharmaceutical product (*e.g.* preformulation, formulation, FDA requirements). 3/31 T. Tr. at 78:25-80-7 (Palmieri); *see also* PDX-8; JTX-4 at CPH_PLD_446.[45]

---

[43] If there is no difference between the prior art and the claims, the patent is invalid for anticipation, which is the "epitome" of obviousness. *See Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983). If the Court finds the '516 patent anticipated, it is necessarily obvious.

[44] Obviousness must be proved by clear and convincing evidence under current Federal Circuit jurisprudence. *PharmaStem*, 491 F.3d at 1360. No deference to the PTO is owed in this case because the PTO's obviousness rejection was not the same as Apotex's claims of invalidity as discussed in Section V(B). *See Tokai Corp. v. Easton Enterprises, Inc.*, 632 F.3d 1358, 1367 (Fed. Cir. 2011) (affirming district court's finding of no PTO deference despite most, but not all, of the prior art cited in defendant's obviousness defense was in front of the PTO).

[45] A person of skill in the art could also have a B.S. degree in pharmaceutics, chemistry, or a related field if they had equivalent industrial and academic experience to be equivalent to the Ph.D. described above. 3/31 T. Tr. at 78:25-80-7 (Palmieri); *see also* PDX-8. A person with medical training, such as an M.D., including training in the treatment of somnolent conditions like narcolepsy or other modafinil-responsive conditions would also be a person

C. Scope and Content of the Prior and Differences From the Claimed Invention of the '516 Patent.

1. Prima Facie Case of Obviousness when Information Lafon Communicated to the Named Inventors is Considered Prior Art.

Similar to the confidential picture in *OddzOn*, Lot 003 modafinil itself (i.e. just the powder, with no information on its particle size) as well as the 100 mg tablets made from that modafinil (M006) were communicated to Cephalon by Lafon by July 23, 1993, and thus qualify as prior art. *See* 122 F.3d at 1401-02 (explaining non-anticipatory communications under § 102(f) can be used in the obviousness inquiry). The question thus becomes, would it have been obvious for one of ordinary skill to achieve an embodiment of the claimed invention if provided this modafinil. *See In re Krank*, 438 F.2d 609, 613 (C.C.P.A. 1971) (claims invalid if they read on some obvious embodiments); *Comcast Cable Commc'ns Corp. v. Finisar Corp.*, 571 F. Supp. 2d 1137, 1145 (N. D. Cal. 2008) ("A single obvious embodiment of a claim is sufficient to invalidate the entire claim even if the claim would also cover not-so-obvious embodiments.") (citation omitted). A person of skill would have been motivated to measure the particle size of this modafinil pursuant to FDA regulations (*see, e.g.,* PTX-16 at AI89453) and determining particle size distribution of this modafinil would be accomplished by routine, conventional methods and yield an embodiment within the scope of the claims.[46] JTX-1 at col. 7:33-42 (describing "conventional methods" for particle size analysis); 3/29 T. Tr. at 96:17-25 (Beach); 4/6 T. Tr. at 64:5-16 (Cooper); 4/5 T. Tr. at 122:17-21 (Grebow). As such, pharmaceutical compositions made from modafinil API having 95% of its particles with a diameter less than 220

---

of skill in the art in October 1994. *Id.*

[46] Neither the 102(f) art or the FDA guidelines were in front of the PTO during prosecution of the '845 and '516 patents.

microns as required by all of the claims would have been obvious to one of skill in the art in October 1994.[47]

2. Prima Facie Case Based on Prior Art Publications Alone

Even if one ignored the prior art Lafon materials and information, the claims at issue would have been obvious to a person of ordinary skill in view of the publicly available prior art publications in October 1994. One of skill in the art would be interested in modafinil because it was shown to be a safe and effective drug for the treatment of narcolepsy that was better than traditional narcolepsy drugs. *See supra* at n. 12. By October 1994, modafinil was also known to be poorly water soluble. *See* 3/31 T. Tr. at 83:4-24 (Palmieri), PTX-27 at AI5606; JTX-4 at CPH_PLD_346 (admitting modafinil's low solubility had been known for 20 years). However, the publicly available literature did not disclose the particle size of modafinil used in prior clinical trials. 3/31 T. Tr. at 123:13-23 (Palmieri); 4/4 T. Tr. at 118:15-24 (Baranski).

In order to formulate modafinil to treat narcolepsy, a person of ordinary skill would have to obtain modafinil from somewhere. One of skill could either purchase modafinil API from Lafon or manufacture it themselves pursuant to the conventional methods described in Lafon's prior art '290 patent. PTX-5 at col. 3:1-39; 3/29 T. Tr. at 122:12-21 (Beach); JTX-1 at col. 9:64-67. One of skill purchasing modafinil API from Lafon in 1994 would have received modafinil that fell within the scope of the claims, rendering them obvious *See supra* at Sections III(B) and

[47] Cephalon has not argued that other claim limitations are separately non-obvious, so the claims should fall together. For completeness, the median particle size limitations of Claims 2 and 8 would be met by the same routine particle size measurement of Lot 003. The dosage limitations in Claims 3 and 9 would are met by the 100mg tablets. It would have been obvious to a person of skill in the art in 1994 to include up to 10-15% excess amount of modafinil in dosage forms made from Lot 003 in light of the 1990 USP (PTX-26), thereby meeting the limitations of Claims 13 and 14. *See* 3/31 T. Tr. at 112:25-114:25, 116:22-117:20 (Palmieri); 4/5 T. Tr. at 146:8-19 (Grebow admitting same). It was also obvious to use the M006 tablets to treat narcolepsy, as one of skill would know that Lafon had established modafinil to be safe and effective at 100-500 mg/day. S*ee supra* at n. 12. Even Cephalon's expert, Dr. Cooper admitted a person of ordinary skill receiving those tablets from Lafon would have used those tablets to treat narcolepsy at the claimed dosage ranges. *See* 4/6 T Tr. at 73:21-74:13 (Cooper).

VI(C)(1). Starting fresh using conventional methods, one of skill would follow the Wadke reference, which specifically teaches that for poorly soluble drugs (like modafinil), one should grind the particles until they are small, preferably between 10 and 40 microns.[48] PTX-6 at AI88870; 3/31 T. Tr. at 95:18-6 (Palmieri). Grinding, as recommended by Wadke, would result in a modafinil drug substance having 95% of its particles with a diameter of less than 220 microns and a median diameter between 1.8 and 66 microns. 3/31 T. Tr. at 107:14-109:4 (Palmieri). One would use this modafinil in a 100 mg or 200 mg tablet as described in the prior art. *See, e.g.*, PTX-17. This renders the composition claims (1-3, 7-9, and 13-14) obvious.[49]

As Dr. Palmieri explained, one of skill would be motivated to follow Wadke's suggestion for particle size because it corroborates well-founded scientific principles regarding the impact of a poorly soluble drugs on drug characteristics. First, Wadke's teaching is consistent with the general rule that a decrease in particle size results in an increase in dissolution rate and/or bioavailability.[50] 3/31 T. Tr. at 77:1-4; 83:8-23; 87:5-94:7; 120:22-122:4; 125:9-128:14 (Palmieri); PTX-6 at AI8869-70; PTX-16 at AI89453-54; PTX-32; PTX-41; *see also* PTX-15 at AI88583 ("[Increased dissolution and bioavailability from reducing particle size] has led manufacturers to produce certain drugs in the forms of micronized powders (particle size 5 μm) to be incorporated into various dosage forms."). Further, it was known that using a smaller,

[48] None of the art in front of the PTO contained a similar general teaching to grind large particles of any new drug substance to 10-40 microns.

[49] One of ordinary skill would have a reasonable expectation that such modafinil would work as an effective treatment for narcolepsy at 100-500 mg daily dosages, so the method of use claims (4-6, 10-12, 16) would have been obvious as well. *See supra* at n. 12.

[50] The classic example of the effect particle size has on dissolution and bioavailability is similar to Cephalon's "discovery" story. In the griseofulvin example, the manufacturer changed its manufacturing protocol to make synthesis of the drug cheaper. It discovered the new method led to a drug that had increased bioavailability as compared to the old method drug. After investigating the reason, the manufacturer discovered the new process reduced the drug's particle size, which led to the increased bioavailability. 3/31 T. Tr. at 85:6-87:8 (Palmieri); PTX-1 at AI88578. While that may have been surprising in 1958, it was well-established in 1994 and any person of ordinary skill in the art would have looked at particle size as a source of any differences in bioavailability.

homogenous particle size distribution allowed for manufacturing advantages, such as better content uniformity in dosage forms (e.g. tablets). 3/31 T. Tr. at 110:11-112:23 (Palmieri); PTX-6 at AI88869. Dr. Palmieri explained that one of ordinary skill would have had a reasonable expectation that these general principles would apply to modafinil, substantiating the motivation to obtain small particle size. 3/31 T. Tr. at 131:18-132:17 (Palmieri).[51]

Further, the person of skill in the art would have been required to confirm that the small particle modafinil it manufactured (or any other drug) acted according to the general expectations with actual dissolution and bioavailability testing pursuant to FDA regulations which were then in effect. *See* PTX-16 at AI89453 (FDA guidelines teaching particle size could "have a large effect on the behavior of the drug product, and significant differences in particle size [could] also affect toxicity."); 3/31 T. Tr. at 118:2-12 (Palmieri on motivation to investigate effect of particle size). This dissolution profile and bioavailability testing is routine laboratory work for those of skill in the art. *Id.* at 128:24-129:14 (Palmieri on routine dissolution studies); *id.* at 130:13-25 (Palmieri on routine bioavailability studies). Because only routine testing would be required to confirm that Wadke described the optimal range for particle size of modafinil, as expected, the claims are obvious. *See In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997) ("[I]t is not inventive to discover the optimum or workable ranges by routine experimentation.") (quoting *In re Aller*, 220 F.2d 454, 456 (C.C.P.A. 1955).

Cephalon will likely argue that only large particle modafinil was being used in the foreign clinical trials, that large particle modafinil was bioavailable, and so there would be no motivation to modify the large particle modafinil to small particle modafinil. All three elements

[51] There are exceptions to these rules, but Apotex need only show a reasonable expectation of success, not absolute predictability for obviousness. *See In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009) ("[O]bviousness does not require absolute predictability of success . . . all that is required is a reasonable expectation of success." (internal quotations omitted)). The general rule establishes a reasonable expectation of success.

are flawed. First, small particle modafinil was being used in the foreign clinical trials. *See supra* at Section III(C). Cephalon's expert Dr. Cooper's opinion, and the PTO's examination of the '516 patent, is wholly based on this incorrect assumption. Put simply, there is no reasonable explanation why Early Lots E-A, E-B, and E-C are considered prior art (the basis for Cephalon's non-obvious argument) when Lot 5/2435, which was also used in foreign clinical trials, is not. The second element is true, but largely irrelevant because small particle modafinil was also bioavailable (and safe and effective). *See supra* at Section III(C). The third element, motivation to modify, is misleading because Cephalon did not modify the particle size of modafinil. *See supra* at Section V(B). Lafon had already modified it years before, at least by 1989. Also, one of skill in the art would be motivated to optimize the bioavailability because it can have commercial advantages, such as increased potency. 3/31 T. Tr. at 128:1-14 (Palmieri); PTX-32; PTX-41; *see DyStar Textilfarben GmbH v. C.H. Patrick Co.*, 464 F.3d 1356, 1368 (Fed. Cir. 2006) ("... the desire to enhance commercial opportunities by improving a product or process is universal-and even common-sensical ...").

D. Any Secondary Considerations Do Not Rebut the Obviousness of The '516 Claims.

Secondary considerations, such as commercial success and unexpected results, are considered in the obviousness analysis. *See KSR*, 550 U.S. at 406. A nexus between the merits of the claimed invention and the evidence of secondary considerations is required in order for the secondary considerations to be given substantial weight in an obviousness determination. *See In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995). "Although secondary considerations must be taken into account, they do not necessarily control the obviousness conclusion." *Pfizer Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007). They do not overcome a strong case for obviousness. *See, e.g., Pfizer*, 480 F.3d at 1370-72; *Dystar*, 464 F.3d at 1371; *see also*

Anderson's Black Rock, Inc. v. Pavement Salvage Co., 396 U.S. 57, 61 (1969) (considering secondary considerations and holding that "those matters without invention will not make patentability"). As demonstrated above, one of skill would have had such a strong motivation to make pharmaceutical compositions of modafinil with modafinil with 95% Critical Value of less than 220 microns and use these compositions to treat sleepiness associated with narcolepsy that no secondary considerations can overcome that showing of obviousness.

1. Supposed Commercial Success

Cephalon may argue commercial success based on one conclusory statement made by Dr. Grebow. *See* 4/4 T. Tr. at 171:13-16 (Grebow); *cf. In re Baxter*, 952 F.2d at 392 ("Baxter's evidence that most of its commercial bags were within the scope of the patent claims is not sufficient to establish commercial success.").[52] Cephalon did not establish a nexus between any commercial success of Provigil® and the claims of the '516 patent because it did not show a clinical difference between large particle modafinil and the claimed small particle modafinil.. *See* 3/30 T. Tr. at 127:16-128:3; 156:11-12; 150:23-151:13 (Feifel); *see J.T. Eaton & Co. v. Atl. Paste & Glue Co.*, 106 F.3d 1563, 1571 (Fed. Cir. 1997) ("the asserted commercial success of the product must be due to the merits of the claimed invention beyond what was readily available in the prior art."). Further, Cephalon's FDA exclusivity from its NDA and the Lafon '290 patent (PTX-5) blocked others from the market, which minimizes the relevance of any commercial success that Cephalon may enjoy. *See Merck & Co., Inc., v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1377 (Fed. Cir. 2005) ("Because market entry by others was precluded on those bases [of a

[52] If Cephalon introduced further testimony, Apotex would have shown that a portion of Cephalon's commercial success stemmed from its illegal off-label promotion of Provigil®, for which it has entered into a criminal plea, and argued that Cephalon should not be able to rely on sales derived from criminal activity to support its patent. *See U.S. v. Cephalon, Inc.* 2:08-cr-00598-HB, at Dkt. No. 2.

prior patent and FDA exclusivity], the inference of non-obviousness . . . from evidence of commercial success, is weak.").

2. Supposed Unexpected Results

Cephalon's "unexpected results" arguments should be given little weight because they are all based on its faulty premise that the foreign trials only used large modafinil. *See supra* at Section V(B). Cephalon should have disclosed that Lot 5/2435 was also used, making it prior art, and then there could be no unexpected results in comparison to that Lot, which falls within the scope of the claims.

Additionally, there was no clinical benefit when comparing small particle modafinil to large particle modafinil. Both were safe and effective at a dose of 200-400 mg/day and had a maximum tolerable dose of 600 mg/day. *See, e.g.*, 3/30 T. Tr. at 150:23-152:18 (Feifel); 4/4 T. Tr. at 119:22-120:4 (Baranski); PTX-18. Indeed, Cephalon's clinical expert provided no testimony that the small particle modafinil was better – if credited, his testimony would only show that at unclaimed dose (i.e. single 800 mg dose) well outside what was recommended (i.e. 100-500 mg daily), small particle modafinil was unexpectedly worse in one patient. 4/4 T. Tr. at 123:2-5, 124:7-10 (Baranski); *id*. at 121:5-122:12, 122:23-123:5; *id*. at 92:23-93:2 (one individual). Apotex's clinical expert Dr. Feifel provided an unchallenged opinion that the '516 patent does not demonstrate increased safety or efficacy of the claimed modafinil, and that there was no data showing a significance difference in bioavailability (based on dog-plasma study). 3/30 T. Tr. at 131:12-24, 150:23-151:9 (Feifel); PTX-96A.[53]

[53] The Shek Declaration discusses bioavailability in humans of modafinil pharmaceutical compositions made with modafinil of different particle sizes. *See* JTX-4A at CPH-FTC 21644, Table 2. Given that there was no significant difference between large and small modafinil in the dog plasma study, it is not surprising or unexpected to have consistency when all the modafinil is small. 3/31 T. Tr. at 146:21-147:13 (Palmieri). The results are further not surprising because they follow the dissolution data, and because a person of skill in the art would expect that bioavailability would not improve below a certain size limit. *Id.*; *see also* PTX-122 (teaching that drugs can have

Further, the dissolution tests in the '516 patent specification do not establish any unexpected results. The dissolution studies compare a single Late lot (L-1) with one or two Early Lots (E-B and E-D). *See* JTX-001 at col. 9:16-52, Figs. 6 and 7. The results of these comparisons are exactly what one of ordinary skill would have reasonably expected: "...You reduce particle size, you get a faster rate of dissolution." 3/31 T. Tr. at 62:14-23 (Palmieri). Also, because the experiments in the '516 patent specification only compare one "late" lot of modafinil (L-1) with "early" lots of modafinil (E-B and E-D), they cannot demonstrate "consistent" dissolution rates or bioavailability across lots of modafinil with 95% Cumulative Values of less than 220 microns. 3/31 T. Tr. at 74:5-14; 76:23-25 (Palmieri).

Finally, the dissolution results in the Shek Declaration (JTX-4A & JTX-4C) are not unexpected because, while the general rule is that decrease in particle size increases dissolution rate, it was also known that at some point you would reach a leveling off point because other forces such as clumping start to nullify further improvement. *See* PTX-6 at AI0088870 (when particles reach "to too small a dimension," it can lead to the API clumping together (i.e. agglomerating); 3/31 T. Tr. at 138:21-139:14 (Palmieri showing how agglomeration results in a lowering of the effective surface area and lead to a flattening or slowing of dissolution rate); *see also* PTX-94 at CPH_PLD_111867 (Cephalon attributing the leveling in the study in Shek to clumping). As such, the dissolution results in the Shek Declaration would not be surprising to a person of ordinary skill in the art. 3/31 T. Tr. at 135:15-136:24 (Palmieri). The level where this anticipated effect would take place is easily determined with routine dissolution studies. *See supra* at Section VI(C)(2). Even if the *in vitro* results in the Shek declaration are unexpected, they cannot overcome the strong case of prima facie obviousness, especially as any such

---

the same absorption into blood (i.e. bioavailability) below a certain "critical particle size (CPS)").

difference did not result in any demonstrable clinical benefit. *See Pfizer*, 480 F.3d at 1370-72; *Dystar*, 464 F.3d at 1371.

VII. The Claims of the '516 Patent are Invalid Under 35 U.S.C. § 112, ¶ 1 for Lack of Written Description.

The written description requirement under 35 U.S.C. §112 is a question of fact.[54] *See Eli Lilly & Co. v. Teva Pharm. USA, Inc.*, 619 F.3d 1329, 1345 (Fed. Cir. 2010). The "test [for written description] requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art. Based on that inquiry, the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed." *Ariad*, 598 F.3d at 1351. Here, if the Court finds that the claims allow for measuring the particle size of modafinil *after* it is manufactured into a finished tablet,[55] the claims are invalid for lack of written description because a person of ordinary skill in October 1994 reading the '845 patent specification would understand that the Cephalon patentees only possessed measuring the particle size of modafinil *before* it was tabletted, i.e. measuring bulk modafinil drug substance (i.e. API). That is because the '845 patent only discloses measuring modafinil powder as in API.[56] Also, one of ordinary skill would not know whether the particle size would be the same before and after formulation. *See* 3/30 T. Tr.

[54] The specification must "contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same ...." 35 U.S.C. § 112, ¶1. This statutory language creates two separate requirements for the patentee—the first is referred to as the written description requirement and the second is the enablement requirement. *See Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

[55] Based on its Supplemental Infringement Contentions (Dkt. No. 339), Apotex expects that Cephalon will argue the claims cover measuring the particle size of modafinil after it has been formulated into a tablet. Apotex disagrees that this can be a "conventional method" as the Court has construed the claims. *See* 3/29 T. Tr. at 105:4-107:2 (Beach); Dkt. No. 455, 8/17/04 Dep. Tr. at 169:1-5 (Ravin); 8/05/04 Dep. Tr. at 52:14-54:2 (Shek). Cephalon presented no opinion on this issue as Dr. Cooper's testimony was properly limited to enablement only. *See* 4/6/11 T. Tr. at 61:20-62:3; 65:25-66:13 (Cooper).

[56] *See* JTX-1, col. 6:37-44; Figs. 1-5; Tables 1 and 2; 4/11 T. Tr. at 107:2-108:7 (Beach). Even outside the patent, Cephalon did not measure particle size of modafinil when it was mixed with excipients or tabletted. *See* Dkt. No. 455, 1/27/04 Dep. Tr. at 93:6-10 (Heacock); 10/27/04 Dep. Tr. at 258:9-12 (Heacock).

at 57:8-15 (Beach); Dkt. No. 455, 1/27/04 Dep. Tr. at 87:15-88:18 (Heacock). Therefore, the construction Cephalon seeks is not supported by the '516 patent specification. *See Eli Lilly*, 619 F.3d at 1345 (the specification only disclosed measurements of bulk API and one of skill reading the specification would not know if the particle size changed before and after formulation).

VIII. Apotex has Standing to Bring its '516 Patent Declaratory Judgment Claims.

Apotex addresses the issue of standing because Cephalon raised it again in its Fed. R. Civ. P. 52(c) motion. *See* Dkt. No. 449-1 at 10. However, this Court has already determined standing twice, and recently ruled that Apotex's GMP issues do not impact Apotex's standing for the '346 patent declaratory judgment claims. See Dkt. No. 224; Dkt. No. 435 at ¶17. The recent ruling is law of the case for the '516 patent because the GMP argument advanced here is the same that was decided. *See, e.g., Cover v. Hydramatic Packing Co*, 1997 WL 196621 (E.D. Pa. Jan. 15, 1997).[57] For the reasons the Court has already addressed, Apotex has standing to pursue its declaratory judgment claims on the '516 patent.

[57] Also, Cephalon recently has agreed that another federal district court has subject matter jurisdiction over Apotex's declaratory judgment claims regarding the '516 patent (as well as the '346 patent) in a case involving Cephalon's follow-on product called armodafinil (Nuvigil®). *See* 2d Am. Jt. Status Rept., In re Armodafinil Patent Litigation, 1:10-md-2200 GMS (D. Del.), Dkt. No. 33, at 3 ("The parties agree that the Court has subject-matter jurisdiction over ... Apotex Defendants' respective counterclaims pursuant to 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202."). This consent to subject matter jurisdiction (which implicitly includes a concession regarding Apotex's standing and the declaratory judgment claims' ripeness) stands in inexplicable contrast to Cephalon's position in this case.

Dated: April 25, 2011

/s/ Martin S. Masar III
Robert B. Breisblatt
Brian J. Sodikoff
Martin S. Masar III
Stephen P. Benson
Jeremy C. Daniel
Christine E. Bestor
KATTEN MUCHIN ROSENMAN LLP
525 West Monroe Street
Chicago, Illinois 60661-3693
Phone: (312) 902-5200

Howard Langer
LANGER GROGRAN & DIVER, P.C.
1717 Arch Street, Suite 4130
Philadelphia, PA 19103
Phone: (215) 320-5661

Attorneys for Apotex Inc.